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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/693,059

10/23/2003

James McSwiggen

03-465-A (400.136)

1557

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06/15/2009

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EXAMINER

PITRAK, JENNIFER S

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

06/15/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/693,059	Applicant(s) MCSWIGGEN ET AL.	
	Examiner JENNIFER PITRAK	Art Unit 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 May 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) ☐ They raise the issue of new matter (see NOTE below);
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
 5. ☒ Applicant's reply has overcome the following rejection(s): Rejection of claims 18, 20-33 under 35 USC 102(e) as anticipated by Fosnaugh, et al. (2003/0143732).
 6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
 The status of the claim(s) is (or will be) as follows:
 Claim(s) allowed: _____.
 Claim(s) objected to: _____.
 Claim(s) rejected: 18, 20-33.
 Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
 10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
 13. ☐ Other: _____.

/Sean R McGarry/
 Primary Examiner, Art Unit 1635

Continuation of 10 and 11. does NOT place the application in condition for allowance because: Applicant's declaration under 37 C.F.R. 1.132 has obviated the rejection of claims 18, and 20-33 under 35 USC 102(e). However, the claims stand rejected under 35 U.S.C. 103(a) as indicated in the rejection. Response to Applicant's arguments follows.

Applicant first argues that the Elbashir reference does not suggest the use of terminally 2'-OMe-modified siRNAs (pages 4-6 of 5/28/09 response). As indicated in the Final Office Action of 02/03/09 on pages 3-4, Figure 4 of the Elbashir reference shows the successful use of 2'-deoxy-modified nucleotides at the ends of siRNA strands and contrasts these end-modified siRNAs with fully 2'-deoxy- and fully 2'-methyl-modified siRNAs which have reduced functionality. From this Figure and the discussion at pages 6881 and 6885 (left column), one of skill in the art would recognize that use of 2'-methyl modifications at the ends of siRNAs would likely produce very similar results as shown for 2'-deoxy modifications. The statement on p.6885, "[M]ore extensive 2'-deoxy or 2'-O-methyl modifications reduce the ability of siRNA to mediate RNA," is interpreted by the Applicant to mean that ANY 2'-O-methyl-modification is detrimental to siRNA function. Examiner disagrees and interprets this phrase in context to mean that both 2'-deoxy- and 2'-O- methyl-modified nucleotides can effectively be used at the ends of the siRNAs, as shown for 2'- deoxy in Figure 4, but not throughout the siRNA.

Applicant next argues that there is no basis for the allegation that Monia teaches the use of two different modifications at the ends of antisense oligonucleotides to enhance stability and that the DNA in Monia's gapmers is not modified. This is not persuasive because, as indicated in the 07/10/08 Office Action on page 5, the Monia reference teaches that the modified oligonucleotides of their invention may contain ONE OR MORE substituted sugar moieties, preferably those listed in column 8, which include 2'-OMe and 2'-MOE (2'-methoxyethoxy) modifications.

Applicant also argues that the number of known stability-enhancing chemical modifications is huge and that there was no teaching or suggestion in the art as to which modifications could be applied to siRNAs. This is not persuasive because from the long list of possible modifications taught by the Monia reference as indicated in Applicant's response on pages 8-9, Monia, et al. actually exemplify the use of the instantly claimed modifications (2'-OMe and 2'-MOE). Although these modifications are used for stabilizing antisense oligonucleotides, one of skill in the art would have been motivated to try such known modifications to enhance siRNA stability. Monia's use of 2'-OMe and 2'-MOE, for example, provides direction for the skilled artisan as to which modifications to apply to siRNAs.